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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,223	12/06/1999	DAVID WALLACH	WALLACH=24	9660

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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/445,223	Applicant(s) WALLACH ET AL.
	Examiner MINH-TAM DAVIS	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8,11,14,15,22-24,29,30,40-49 and 51-53* is/are pending in the application.

4a) Of the above claim(s) *14,15,22,29,30,40-43 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8,11,23,24,44-48 and 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

RESTRICTION

Applicant argues that the Examiner disregards example 17 of the PCT Administrative Instructions on the ground that it is only an example and that there is no indication that a DNA and corresponding protein have to be examined together because they do not share a common structure. Applicant argues that there is nothing in any of the Administrative Instruction that state that the protein and DNA must share a common structure, and that is impossible, of course, to assume that such was ever contemplated by Example 17. Applicant argues that DNA and the corresponding protein cannot share a common structure, that it is against the laws of nature, and that surely the authors of Example knew that . Applicant asserts that the special technical feature is the novel protein and that DNA that corresponds thereto share the same special technical feature, as does the method of use of said protein.

Applicant's arguments set forth in paper No.16 have been considered but are not deemed to be persuasive for the following reasons:

After review and reconsideration, the Examiner agrees that Example 17 should be applied to particular cases, claiming a protein X and DNA encoding protein X.. However, Example 17 cannot be applied for the instant application, and claims 40-43,

drawn to the B1 protein are not rejoined with the presently examined B1 polynucleotide claims for the following reasons:

1) The claims of the instant application are not drafted in the format of Example 17, i.e. in Example 17, the claims are drawn to a) a protein X and b) DNA sequence encoding protein X, whereas in the instant application, the claims are drawn to a) a DNA sequence comprising SEQ ID NO:2, and b) a protein encoded by a DNA sequence comprising SEQ ID NO:2.

2) The encoded proteins of claims 40-43 could have several forms of proteins, the structure of which does not share the same or common property with the encoding DNA sequence comprising SEQ ID NO:2, or with the antisense of part of an mRNA sequence corresponding to said DNA sequence. Thus the encoded proteins and the claimed encoding DNA sequence comprising SEQ ID NO:2 or the antisense of part of an mRNA sequence corresponding to said DNA sequence do not share the same technical feature.

3) According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The claimed polynucleotide sequence encoding an analog or a fragment of the encoded protein, which analog or fragment potentiates cell death do not share the same technical feature with the encoded protein, because potentiating cell death is an activity known for several proteins in the art, such as BAX or various caspases (see specification on page 6, last paragraph, and page 7, last paragraph, bridging page 8), and thus potentiating

cell death is not a contribution over the prior art and is not considered a special technical feature.

Further, methods of use of said protein in claims 14-15, 49 are not rejoined and examined, because said methods of use are additional methods of use of the second product, the encoded protein. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims (see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).).

The requirement is still deemed proper, and was made FINAL, for reasons set forth above and in previous Office action.

Accordingly, claims 5-8, 11, 23, 24, 44-48, 51-53 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER

Claims 24, 51-53 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant asserts that the amendment now obviates the rejection.

Applicant's arguments set forth in paper No.16 have been considered but are not deemed to be persuasive for the following reasons:

The specification does not teach an oligonucleotide molecule "consisting of" an antisense sequence of at least part of an mRNA sequence corresponding to a DNA sequence comprising SEQ ID NO:1 or an analog or fragment thereof, which analog or fragment potentiates cell death.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claims 5-8, 11, 23, 24, 44, 46, 51-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 5-8, 11, 23, 24, 44, 46, 51-52 are drawn to a DNA sequence encoding a polypeptide comprising SEQ ID NO:1, or "an analog fragment thereof having no more than ten changes in the amino acid sequences of said DNA sequence, each said change being a substitution, deletion or insertion of a single amino acid, which analog potentiates cell death".

The specification does not disclose the limitation of "an analog that has no more than ten changes in the amino acid sequences of said DNA sequence, each said change being a substitution, deletion or insertion of a single amino acid, which analog potentiates cell death".

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

1. Claims 5-8, 11, 23, 24, 44-48, 51-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated cDNA sequence encoding a polypeptide comprising SEQ ID NO:1, does not reasonably provide enablement for a "DNA" sequence encoding a polypeptide comprising SEQ ID NO:1, an analog or fragment thereof, which analog or fragment potentiates cell death, and an antisense sequence thereof . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 5-8, 11, 23, 24, 44-48, 51-53 are drawn to a "DNA" sequence encoding a polypeptide comprising SEQ ID NO:1, an analog or fragment thereof, which analog or fragment potentiates cell death, and an antisense sequence thereof.

Claims 5-8, 11, 23, 24, 44-48, 51-53 encompass a genomic DNA sequence encoding a polypeptide comprising SEQ ID NO:1, an analog or fragment thereof, which analog or fragment potentiates cell death, and an antisense sequence thereof.

The specification discloses that the clone comprising the claimed polynucleotide sequence is isolated from cDNA libraries (Example 1, last three sentences of the last paragraph on page 52).

One cannot extrapolate the teaching of the specification to the scope of the claims because of the following reasons: The specification fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently

encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (Harris et al. J. of The Am Society of Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art and one of skilled in the art cannot predict the structure of the claimed DNA sequences based on the structure of the disclosed cDNA sequence encoding the polypeptide comprising SEQ ID NO:1.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

2. Claims 5-8, 11, 23, 24, 44, 46, 51-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated cDNA sequence encoding a polypeptide comprising SEQ ID NO:1, does not reasonably provide enablement for an analog of a DNA sequence encoding a polypeptide comprising SEQ ID NO:1, which analog potentiates cell death. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 5-8, 11, 23, 24, 44, 46, 51-52 are drawn to a DNA sequence encoding a polypeptide comprising SEQ ID NO:1, an "analog" thereof having no more than ten changes in the amino acid sequences of said DNA sequence, each said change being a

substitution, deletion or insertion of a single amino acid, which analog or fragment potentiates cell death.

An analog can be interpreted as any chemical or genetic modification. The specification does not teach chemical or genetic modification of SEQ ID NO:1, because it does not teach how to make such diverse analog encompassed within the scope of the claims.

Applicants have not enabled these types of DNA sequences encoding the modified proteins in the specification.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. Such unpredictability would equally apply to DNA sequences which encode proteins. For example, replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al. Journal of Cell Biology, 1990, 11: 2129-2138, of record). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252, of record). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601, and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54, all of record). These references demonstrate that even a single amino acid

substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

In view of the above unpredictability, one of skill in the art would be forced into undue experimentation in order to perform the claimed invention as broadly as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

May 2, 2003